# Chapter 12 Ecosystems and Vector-borne Disease Control

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### Main Messages

Actions to reduce vector-borne diseases can result in major health gains and relieve an important constraint on development in poor regions. Vectorborne diseases cause approximately 1.4 million deaths per year, mainly from malaria in Africa. These infections are both an effect of, and contribute to, poverty.

Ecosystems provide both the "disservice" of maintaining transmission cycles with cross-infection of humans and the "service" of regulating those cycles and controlling spillover into human populations. The balance between these services and disservices is influenced by the availability of suitable habitat for vectors and of reservoir hosts of infection. Transmission cycles are generally kept in a degree of equilibrium by density-dependent processes such as acquired immunity to infectious disease and by limits on the carrying capacity of the habitat to support insect vectors and reservoir hosts.

Human activities that alter natural ecosystems also affect the transmission cycles of vector-borne infectious diseases. Human settlement and deforestation patterns; the development of dam, drainage, and agricultural irrigation schemes; and climate change are all drivers influencing patterns of disease distribution and incidence. Policies that influence population size, migration, patterns of energy production/consumption, food production, and overall demand for natural resources will have significant effects on transmission of infectious agents and associated consequences in terms of disease. These changes may lead to the destabilization of natural equilibria, improved conditions for disease transmission, and disease outbreaks/elevated risks to humans, or alternatively, to the disruption of the disease transmission cycles and decreased incidence.

Present institutional structures tend to promote a narrow, sectoral approach to intervention for individual diseases. Inter-sectoral and interdisciplinary approaches can help control vector-borne diseases while maintaining ecosystem equilibrium (medium confidence). There are numerous examples of health sector institutions working together to mobilize funds and deploy appropriate interventions to significantly reduce transmission of specific infectious diseases. These include international programs that have dramatically reduced the burden of Chagas disease in South America and onchocerciasis in West Africa and created new initiatives on filariasis, schistosomiasis, African trypanosomiasis, and guinea worm. These programs often incorporate monitoring and successful management of environmental impacts. In most countries, however, the health and environment sectors are clearly divided, with little coordination of approaches to epidemiological and environmental monitoring, vector control, and associated energy, agricultural, housing, and forestry policies to further human well-being.

Actions taken to reduce the transmission of infectious diseases often have effects on other ecosystems services. Integrated vector management strategies permit a coordinated response to both health and the environment. IVM strategies use targeted interventions to remove or control vector breeding sites, disrupt vector lifecycles, and minimize vector-human contact, while minimizing effects on other ecosystem services. IVM is widely viewed as a useful approach and is increasingly promoted by international organizations (for example, the World Health Organization and the United Nations Environment Programme) and by national governments.

Environmental management and biological and chemical interventions can be highly cost-effective and entail very low environmental impacts (medium confidence). Potential interventions include use of fish and bacterial larvicides such as *Bacillus thuringiensis israelensis* (Bti) and chemical application methods that cause minimal disruption to broader ecosystems, such as insecticide-treated bed nets and indoor residual spraying. In the case of malaria, better design, management, and regulation of dams and irrigation schemes and water drainage systems can potentially reduce breeding sites, particularly in peri-urban areas and areas of less intensive transmission. In several settings, vector-human contact may potentially be reduced by location of human settlements away from major breeding sites and through the strategic management of diversionary hosts such as cattle (zooprophylaxis).

IVM will be most effective when integrated into development approaches that also improve socioeconomic status (*high confidence*). There is strong evidence that poverty and malnutrition increases vulnerability to the effects of vector-borne disease. For example, improved socioeconomic status facilitates the purchase of bed nets and other forms of personal or household protection for malaria. Better housing conditions are associated with reduced transmission of some vector-borne diseases. Disease control measures should therefore be part of integrated development strategies that improve all aspects of well-being.

Social and behavioral responses can help control vector-borne disease while also improving other ecosystem services (medium confidence). Public health education forms an increasingly important component of management programs and initiatives, raising awareness about individual and communal actions that may control vectors, their breeding sites, prevent disease transmission, and provide access to treatment. Aside from directly impacting disease control, health education gives individuals greater control over their lives and therefore promotes cultural services. However, it is difficult to bring about long-term behavioral changes in populations, that is, community programs of systematic and constant management of key breeding sites/containers, unless behavioral changes are reinforced by social or individual incentives/ benefits.

New "cutting-edge" interventions, such as transgenic techniques to reduce or eliminate the capacity of some vector species to transmit infectious diseases, could be available within the next 5 to 10 years (medium confidence). However, consensus is lacking in the scientific community on the technical feasibility and public acceptability of such an approach. Transgenic techniques include the production of genetic constructs that block the expression of the pathogens (the infectious agents that can cause clinical disease) and their incorporation into gene-drive mechanisms such as transposable elements or Wolbachia endosymbionts that could spread them throughout mosquito populations. Because genetic replacement targets only individual mosquito species and aims to decrease vector competence rather than reduce population size, it has the potential to be an intervention with minimal environmental impact. There is no a priori reason to expect either that the genetic construct will affect other important characteristics of the target mosquito population (such as the ability to transmit other diseases) or that it will cross into other species. However, significant technical and logistical challenges must be overcome in order to establish an operational program. In many countries, there is also significant public opposition to transgenic products such as foods. Unless perceptions change, there is likely to be similar resistance to the release of transgenic insects.

Environmental modification not directly aimed at vector control often affects the ecosystems regulating vector-borne disease transmission (*high confidence*). The specific effects will depend on local transmission ecology. Interventions such as deforestation may cause decreases in disease incidence in one location but increases elsewhere or even increases in a different form of the same disease within the same location. Similarly, the effects of any ecosystem change will vary over time. For example, irrigation schemes in Sri Lanka initially caused an increase in malaria incidence but this later decreased due to replacement of the original *Anopheles* species with a less efficient vector, along with improved socioeconomic conditions and medical care. Assessments of local environmental, epidemiological, and socioeconomic conditions are necessary before making such modifications. This may entail studies at the cutting edge of science in determining vector species genetics and transmission potential.

The adoption of a longer-term and more holistic view of the interactions between ecosystems and infectious diseases would help to ensure sustainable benefits to human well-being (*high confidence*). The current division of responsibilities among institutions means that assessment and programmatic responses are within narrow disciplinary or sectoral frameworks. The health sector usually makes reference to scientific/logistical criteria (for example, availability of programmatic resources, immediate effectiveness in reducing disease, cost-effectiveness), and social-cultural considerations (for example, public and political feasibility). Such approaches are not ideal for a broader inter-sectoral policy that considers the effects of a particular health strategy on other ecosystem services or, conversely, the impacts of environmental and development strategies on disease transmission. An ecosystem assessment or ecohealth approach examines strategies from a trans-disciplinary perspective, considering direct and immediate effects on disease, as well as longer-term or indirect effects that may occur via alterations to ecosystems.

### 12.1 Introduction

#### 12.1.1 Current Status of Vector-borne Disease

Vector-borne infections are major killers, particularly of children in developing countries. Over the past decade, more comprehensive and transparent methods of measuring health have improved understanding of the importance of these diseases. The World Health Organization reports annually on the numbers of deaths and DALYs (disability adjusted life years, a composite measure of health status combining premature death and sickness during life), by disease category in different regions of the world (for example, WHO 2004a). Despite technological advances and increasing affluence in many regions, vector-borne infectious diseases remain amongst the most important causes of global ill-health.

This burden is concentrated in the poorest regions of the world (see MA *Current State and Trends*, Table 14.1, Figure 14.1). For example, malaria alone is responsible for approximately 11% of the total disease burden in Africa, while all vector-borne diseases combined are responsible for less than 0.1% in Europe. Vector-borne disease is not only an outcome but a cause of poverty. Countries with intensive malaria have income levels averaging only 33% of those without malaria, even after accounting for the effects of tropical location, geographic isolation, and colonial history (Gallup and Sachs 2001).

#### 12.1.2 Future Projections

The global burden of disease methodology has also been used to project the likely changes in disease impacts between 1990 and 2020 (Murray and Lopez 1996; Lopez and Murray 1998). These projections suggest that continuing economic development will be associated with an epidemiological transition period. Diet and lifestyle changes associated with growing urbanization as well as increased substance abuse, environmental degradation, population growth, and levels of regional and local conflict are expected to lead to a surge in non-communicable diseases, including those associated with cerebrovascular events, depressive illness, conflictrelated conditions, road traffic accidents, and cancers.

Infectious diseases are projected to decrease in relative importance, with only malaria expected to represent a very significant proportion of the global burden of disease, and even this disease falling from a ranking of 11th to a predicted 26th. However, this may be an overly optimistic projection of progress against infections. For instance, projections made in 1996 for the burden of disease from malaria and dengue in 2000 were subsequently found to have underestimated the true burden by 32% and 11%, respectively (WHO 2001). Drug resistance, population movement, and the effects of the HIV/AIDS pandemic on immune status threaten the global effort to contain infectious diseases.

Whatever the precise nature of future trends, firm response measures to control infectious disease will be required for the foreseeable future and these measures will inevitably affect or interact with other ecosystem services. In addition, growing human populations and increased demand for ecosystem services/natural resources means that there will be continuing, and possibly increasing, human interactions with the natural processes that influence infectious disease transmission.

#### 12.1.3 Scope and Purpose of the Assessment

All diseases, from infections to cancer and cardiovascular disease, are influenced to some degree by the environment. However, this chapter focuses on vector-borne infectious diseases for the following reasons.

- These diseases are especially ecologically sensitive, since environmental conditions, such as temperature, affect both the infectious pathogens (for example, malaria parasites or dengue viruses) that, depending on the interaction with human hosts, have the potential to cause clinical disease and the insects and other intermediate hosts that transmit them.
- Many such infections are directly linked to natural ecosystem types (such as forests and wetlands) considered elsewhere in this assessment.
- Such infections are strongly linked to poverty, and therefore other aspects of human well-being.

In addition, as noted above, vector-borne diseases are among those infectious diseases with the highest disease burden today, and may be expected to represent the highest proportionate disease burden in the future. Responses related to other ecosystemhealth interactions are covered in Chapter 16 of this report.

The assessment examines potential policy responses that may reduce the burden of infectious vector-borne diseases, from an ecosystem perspective. In this perspective, ecosystem impacts from the policy responses also are considered, and the preservation of ecosystem services is viewed as a priority. As the chapter focuses on policy responses, there is only a brief introduction to the ecological concepts underpinning the relationships between environmental states and disease transmission. A more detailed description of these interactions, including for example the effects of "systemic" ecosystem disruption on complex transmission cycles involving multiple hosts, is given in MA *Current State and Trends*, Chapter 14.

It should also be noted that vector-borne disease infections are influenced by a wide range of factors not directly related to ecosystem services. These include the provision of basic public health services to prevent, detect, and treat disease, as well as "good governance" ensuring that these services are responsive to citizens needs and that resources for disease control are not lost to corruption and inefficiency. While recognizing the importance of these influences, the chapter focuses on more direct links between disease control and the environment. It includes:

 an overview of the basic ecosystem mechanisms and environmental drivers that influence and regulate vector-borne disease transmission;

- an overview of global trends (for example, trade, globalization, economic development, and urbanization) that act as indirect drivers affecting the condition of ecosystems and vector-borne disease;
- a review and assessment of integrated vector management strategies, which provide a comprehensive approach for integrating effective disease control with consideration of other ecosystem services.
- a description of social and behavioral responses to vectorborne disease management, particularly in the context of sustaining integrated policies; and
- a discussion of inter-sectoral cooperation in promoting ecosystem approaches to vector-borne disease management.

# 12.2 Environmental Drivers, Ecosystem States, and their Effects on Vector-borne Disease

# 12.2.1 The Relationship between Ecological Conditions and Vector-borne Disease

An ecosystem perspective on the risks to humans from vectorborne disease and vector management requires an appreciation of the role played by broad environmental trends and by local ecosystems in sustaining vector habitats and facilitating disease transmission.

The transmission of vector-borne diseases is governed by the same principles of population dynamics as other ecological systems. Probably the most important governing concepts are the reproductive rate (often termed r) of vectors and parasites and the carrying capacity (K) of the local habitat for each of these entities (Thomson et al. 2000). Both are influenced by broad environmental conditions. For example, in the case of malaria in an African village, seasonal temperatures affect the reproductive rate of *Anopheles* mosquitoes and of the *Plasmodium* parasites within them. Precipitation influences the availability of aquatic breeding sites.

Together, such factors influence the maximum number of adult mosquitoes that can be produced and sustained in the local environment in a given time. While these large-scale climatic factors are important, their influence in any particular setting also depends upon local characteristics. For instance, both temperature and breeding site availability are also a function of local topography and vegetation. Finally, humans are an integral part of this system. Agricultural practices will influence land use and the availability of animals that may provide blood meals for mosquitoes (along with or instead of humans). Targeted vector control interventions may reduce vector abundance and longevity vector habitats and/or vector biting rates on humans and thus prevent disease transmission, even in otherwise optimal environments. The same environmental conditions that are affected by local habitat factors also determine the vector-carrying capacity of the ecosystem, the point at which vector abundance is limited by densitydependent processes (for example, predation and competition for food).

From a public health perspective, ecosystems provide both "disservices" by maintaining pathogen transmission cycles, including cross-infection of humans, as well as the "service" of regulating those cycles in some degree of natural equilibrium. This state of equilibrium prevents even more explosive human disease outbreaks. (See MA *Current State and Trends*, Chapter 14.) The balance of ecosystem services and disservices depends on the nature of human interactions with the various ecosystems and the extent to which these enhance services and eliminate or manage disservices.

#### 12.2.2 Global Trends as Indirect Drivers

When considering "responses" to manage infectious diseases, it is important to recognize that the human actions that have the most profound effects on disease transmission are often not directly aimed at vector-borne disease control. (See Figure 12.1.)

As countries develop, the transition from high-birth, highdeath rate societies to low-birth, low-death rate societies, without concurrent planning programs, has led to rapid population expansion. Coupled with economic growth, this has led to new demands for energy and transport and for food and natural resource products. All of these function as underlying driving forces of environmental change (McMichael 2001). As a result of such drivers, there is consequent expansion of agricultural production, water management and irrigation schemes, hydroelectric dam construction, deforestation, urbanization, and generally greater exploitation of natural resources. All these create new pressures on ecosystems that, in turn, have profound impacts on vector habitats, the carrying capacity of the environment for vector populations, and infectious disease transmission (Molyneux 1997, 2003).

The environmental pressures generated by human activities may act through direct and/or complex mechanistic pathways, and their impacts are therefore situation-specific. The results of such processes may be trade-offs, where interventions to increase an ecosystem service are offset by increasingly frequent or severe disease outbreaks in the human population. This is illustrated by the example of dengue, transmitted by mosquitoes of the genus Aedes (mainly Aedes aegypti and to a lesser extent Aedes albopictus), primarily in urban areas. Rapid urbanization, the accumulation of water-retaining waste products such as plastic containers and tin cans, and increased domestic water storage, for example in large open drums (Gubler 1997), have increased the availability of Aedes breeding sites. Increased international travel has led to the mixing of different strains of the disease, causing more severe clinical symptoms in individuals exposed to more than one strain (Halstead 1988). Overall, the burden of dengue has increased rapidly in recent years and is a major problem even in some of the most affluent and developed settings in tropical regions, for example, Singapore (Wilder-Smith et al. 2004).

Table 12.1 describes how exploitation of some ecosystem services (mining and irrigation) has led to detrimental impacts on malaria transmission, specifically the ratio of infections with the relatively more pathogenic *Plasmodium falciparum* to the more benign *Pl. vivax*.

The long-term positive or negative effects of ecosystem changes may emerge some time later, often complicating initial assessment of the likely ecosystem impacts of development. Conversion of forest to agricultural land in Sri Lanka initially led to outbreaks of malaria, but over time these have declined considerably. (See MA *Current State and Trends*, Chapter 14.) In contrast, deforestation for wood extraction in Latin America was initially considered to disrupt the transmission cycle of cutaneous leishmaniasis, with associated reductions in transmission of the disease to humans (Sampaio 1951). However, over several decades there was a resurgence in disease transmission, particularly among women and children, as sand-fly vectors became abundant in domestic and peri-domestic habitats (Walsh et al. 1993; Campbell-Lendrum et al. 2001).

Some environmental changes triggered by human activities impact on vector habitats, hosts, or disease transmission, in ways that are even more diffuse and difficult to predict accurately. This

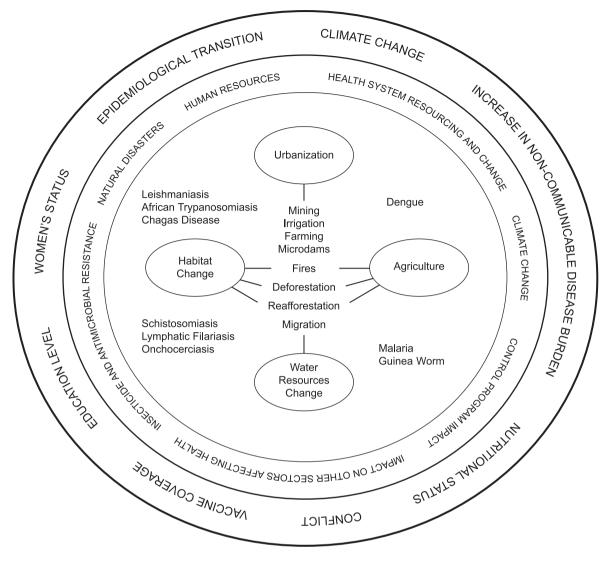


Figure 12.1. Indirect and Direct Influences on Vector-borne Disease Transmission (Molyneux 2003)

# Table 12.1. Examples of Anthropogenic Change Leading to Increases in Plasmodium falciparum: P. vivax Ratios

Location	Anthropogenic Changes	Reference
Tajikistan	health systems disruption, conflict migration, chloro- quine resistance in <i>Plasmo- dium falciparum</i>	Pitt et al. 1998
Afghanistan/ Pakistan	chloroquine resistance in <i>P. falciparum</i>	Rowland and Nosten 2001
Thar Desert, Rajasthan, India	irrigation on large scale; establishment of <i>Anopheles</i> <i>culcifacies</i> -efficient <i>P. falciparum</i> vector and dominance over <i>An. ste-</i> <i>phensi</i> , a poor vector	Tyagi and Chaudhary 1997
Amazonia, Brazil	new breeding sites for effi- cient vectors <i>An. darlingi</i> through mining, deforesta- tion, road building	Marques 1987

includes, for example, the effects of disruption of ecological community structure on transmission dynamics of pathogens such as *Borrelia burgdorferi*, which is transmitted through multiple animal reservoir hosts and can cause Lyme disease in humans. As described in MA *Current State and Trends*, Chapter 14, this can in some cases lead to breakdown in ecological community structure and disruption of natural regulation, with increasing risk to humans. Similarly, it is generally accepted that the use of fossil fuels for energy production has caused changes in global climate (IPCC 2001). This is likely to have influenced the population biology of both disease vectors and pathogens throughout the world, with associated effects on clinical disease in humans (Patz et al. 2003), although in any one site, these influences may be relatively small compared to those of other ecosystem changes (Kovats et al. 2001; Reiter 2001; Hay et al. 2002).

Analytical techniques to estimate the human health risks of such widespread and pervasive ecosystem changes are improving (for example, Zavaleta, 2004) but they can only provide very approximate guidance. They also tend to exclude effects that have only a low probability of occurrence in any one location but potentially devastating consequences. This includes, for example, the possibility that human disruption of natural ecosystems may lead to emergence or re-emergence of important vector-borne diseases that can spread rapidly through the human population, as has occurred for other infectious diseases such as SARS (Severe Acute Respiratory Syndrome) and HIV/AIDS, both probably introduced to human populations through consumption of wild animals. This is a particular risk in areas that combine a high rate of development and ecosystem change with a high population density, such as China. Such low-probability large-consequence events argue in favor of responses that reflect the precautionary principle, as described in principle 15 of the 1992 Rio Declaration on Environment and Development (at the United Nations Conference on Environment and Development Rio de Janeiro, 1992) as-"Where there are threats of serious or irreversible damage, lack of full scientific uncertainty shall not be used as a reason for postponing cost-effective measures to prevent environmental degradation." In practical terms, this could include strengthening environmental protection and surveillance of ecosystems as a precautionary measure to reduce the risks of disease outbreaks.

While there are often trade-offs between disease control and protection of other ecosystem services, there are also potentially synergies where ecosystem changes for other purposes lead to disruption of the vector-borne disease transmission cycle and decreased risks to humans (Patz et al. 2000). One example is the draining of wetlands to expand agricultural production in Europe in the nineteenth and twentieth centuries. This removed large areas of potential breeding sites for Anopheles mosquitoes and therefore played an important role in reducing malaria transmission (Jetten and Takken 1994; Reiter 2000; Kuhn et al. 2003). More generally, increased affluence and better housing and education can reduce transmission of a wide range of diseases even when they are accompanied by ecosystem disruption. Examples include increasing wealth from irrigated agriculture leading to greater ability to purchase antimalarials in Africa (Ijumba et al. 2002) and better housing reducing exposure to malaria infections in Sri Lanka (for example, Gunawardena et al. 1998), lower rates of dengue on the more affluent U.S. side of the Mexico-U.S. border (Reiter et al. 2003), and reduced risk of Chagas disease following house improvement in Latin America (for example, De Andrade et al. 1995).

#### 12.2.3 The Importance of Development Policies

Global, regional, and national development programs, designed to increase material well-being and alleviate poverty, have indirect and diffuse but nonetheless profound influences on infectious diseases. For instance, policies to increase trade can lead to increased deforestation and irrigation, with consequent impacts on vectorborne diseases.

In cases where trade and development policies are effective in reducing poverty, they may also protect against vector-borne disease, as higher socioeconomic status in general may increase individual and community capacity to control infectious diseases. Conversely, international policies that increase the volume of trade, energy use, urbanization, and transport, while failing to alleviate poverty or improve health may exacerbate the risk of vector-borne disease transmission.

Over the past twenty years, there have been greater efforts to integrate international development agendas with concerns over the environment, ecosystems, and health. There is increasing recognition that the link between poverty and vector-borne disease also means that the poorest populations would benefit proportionately more if development had a pro-poor focus that also addresses health and environment in an integrated manner (Gwatkin et al. 1999).

The Rio de Janeiro Earth Summit in 1992 and the Johannesburg World Summit on Sustainable Development in 2002 endorsed Agenda 21 as a comprehensive plan of action for sustainable development while protecting natural resources. Under this guiding principle, a series of internationally negotiated environmental conventions address specific themes such as the protection of biological diversity, regulation of hazardous toxic substances, and combating desertification and anthropogenic climate change. The Millennium Development goals set targets for measurable improvements in development and human and ecosystem health. Several of these goals have relatively direct links to infectious disease transmission, particularly the target of (1) halting and beginning to reverse the spread of HIV/AIDS and the incidence of malaria and other major diseases and (2) halving the proportion of people without sustainable access to safe drinking water by 2015. Other goals will have indirect effects on infectious disease. These include measures to ensure environmental sustainability and the greater use of indicators tracking forested land area and emissions of gases that contribute to climate change and ozone depletion. Although it remains to be seen whether these are feasible, the MDGs at least define specific targets that, if achieved, would represent clear improvements in human health and well-being.

# 12.3 Specific Responses to Vector-Borne Disease in an Ecosystems Framework

This section considers policies and strategies for vector-borne disease management. In particular, it assesses the emerging relevance of integrated vector management, which provides a conceptual approach, along with environmental management and other tools for controlling disease, within an ecosystems framework. A parallel but interrelated track relates to emerging scientific knowledge as well as behavioral and social changes that may contribute to better disease management. Case studies are used to illustrate important features of the different types of responses.

#### 12.3.1 Integrated Vector Management

There is increasing recognition that in the developing countries that suffer the greatest burden of vector-borne disease the trend toward decentralization of decision-making, and the limitations of disease-specific control programs, including the scarcity of technical skills and resources, necessitates a flexible approach to selecting control tools.

In response, there have been rapid developments in defining integrated vector management strategies. IVM strategies have parallels with integrated pest management systems used in agriculture, where the adverse environmental and health effects of pesticides, and the development of resistance, stimulated the flexible use of all methods that have an impact on the pest problem. Such integrated approaches help to preserve ecosystem integrity and encourage the propagation of natural enemies of pest species such as pathogens and predators. An important selling point of this approach is that economic analyses have shown IPM to be more cost-effective than heavy reliance on insecticides, even ignoring the added benefits of reduced environmental contamination.

The principles of IVM can be summarized as seeking to "Improve the efficacy, cost-effectiveness, ecological soundness and sustainability of disease vector control. IVM encourages a multidisease control approach, integration with other disease control measures and the considered and systematic application of a range of interventions, often in combination and synergistically" (WHO 2004b). IVM works on the premise that effective control requires the collaboration of various public and private agencies and community participation rather than exclusive action by the health sector. It entails the use of a range of interventions of proven efficacy, separately or in combination. This serves to maximize costeffectiveness and extend the useful life of insecticides and drugs by reducing the selection pressure for resistance development.

IVM harnesses precise scientific knowledge of the vector ecosystem and its interrelationship to human ecosystems to address the following issues in more environmentally sustainable ways. IVM typically uses four approaches, as appropriate, and in an interrelated manner:

- environmental management, including modification or manipulation of the environment;
- biological control methods, including bacteria and larvivorous fish;
- chemical control methods, including targeted indoor residual spraying, space spraying and larviciding (Walker 2002; WHO 2003; see also Box 12.1); as well as
- social and behavioral measures to decrease suitability for transmission.

Table 12.2 summarizes the main types of control interventions used within an IVM strategy.

Each of these interventions has different types of interactions with other ecosystem services. Table 12.3 maps the main linkages between interventions to control vector-borne disease (including vector control, prevention, and curative measures) and other ecosystem services in the MA framework. In each case, the direction of the arrow gives a rough indication of whether the intervention generally has a greater capacity to increase or decrease the provision of the various services. The following sections examine the more direct interactions in greater detail.

# 12.3.2 Environmental Management/Modification to Reduce Vector and Reservoir Host Abundance

The practice of using environmental management to reduce the capacity of local habitats to maintain populations of disease vectors

predates the development of insecticides. Considerable success was achieved by draining swamps to remove larval breeding sites of *Anopheles* mosquitoes (Pontine Marshes in Italy) and by the use of oil to prevent larval mosquito respiration. *Glossina* (tsetse flies) have been controlled by the selective destruction of savanna and riverine forest habitats together with the destruction of host animals as well as by trapping using sticky materials on the backs of men or by attraction to visual baits since at least the beginning of the previous century.

There has been resurgent interest in environmental management techniques in recent years, stimulated partly by concerns over the sustained effectiveness and environmental consequences of insecticide use. For example, a major motivation for controlling dengue by removing, covering, or treating larval sites in and around houses has been the appreciation that outdoor application of insecticide often has poor penetration into the domestic resting sites of the vectors, has only transient effects, and is logistically demanding (Newton and Reiter 1992).

The capacity of environments to maintain vectors can be reduced by long-term physical changes, often termed environmental modification (WHO 1982; Walker 2002). This may not be the most effective approach in all epidemiological situations. For example, in many highly endemic areas for malaria, using residual insecticide spray to cause even a small increase in the mortality of adult vectors should have a disproportionately large impact on disease transmission. This is likely to outweigh the effect of the same proportional reduction in larval breeding sites.

The effectiveness of environmental management depends on how well the particular intervention is matched to the ecology of the particular disease. Large-scale modification projects tend to require significant initial investments in construction and may be effective only where the targeted area contains the overwhelming majority of breeding sites. Local modifications may also be ineffective where there are alternative breeding sites near human habitations (Mutero et al. 2004), as is the case for malaria in much of rural sub-Saharan Africa. Overall, "accidental" habitat modifica-

#### BOX 12.1

#### Indirect Policy Drivers of Vector-borne Disease: Uganda

In Uganda, cattle are typically treated with chemical pesticides, particularly synthetic pyrethroids, to prevent transmission of two types of vector-borne disease, namely, the tick-borne East Coast fever, which infects cattle, and African trypanosomiasis (sleeping sickness). The latter is transmitted by tsetse flies, with different subspecies of the *Trypanosoma* parasite causing disease in humans and cattle.

Indigenous species of East African cattle are typically more resistant to East Coast fever caused by *Thyleria parva*; they are trypanotolerant, and therefore may require fewer chemical applications. However, there has been increased development of exotic cattle breeds, which reproduce more quickly and yield more milk than native species. The acquisition and raising of livestock for milk production has become an important householdbased economic activity for many poor Ugandans. Since the same synthetic pyrethroids that are used in livestock management are also used in malaria control, this has implications for human disease control efforts.

In a project sponsored by the Systemwide Initiative on Malaria in Agriculture, and funded by the Canadian-based IDRC, researchers are exploring whether the synthetic pyrethroid treatments, when strategically used on cattle, may also provide some protection against malaria infection in humans. This has been the case in some settings in South and West Asia (Hewitt and Rowland 1999; Rowland et al. 2001), and may be particularly relevant in ecosystems with zoophilic vectors, which feed upon cattle as well as humans. A second, related, question is whether the very frequent and widespread use of synthetic pyrethroids on cattle or in agriculture in general might contribute to vector resistance to the chemicals in the long term. This could potentially decrease their effectiveness in bednets, where they are also widely used. Policymakers are also concerned with how the use of chemicals on cattle for vector control may impact the broader ecosystem.

Finally, there is a national development interest in Uganda in promoting the development of a cattle industry, including native cattle breeds, which yield good quality meat and are more fly/tick resistant, thus requiring fewer pesticide/acaricide applications. Genetically mixed cattle breeds may also provide better milk production than the local species, while also providing higher levels of resistance to certain types of vector-borne disease. A joint project of the WHO/UNEP-sponsored Health and Environment Linkages Initiative (HELI) is supporting an inter-sectoral assessment of livestock industry development, chemical use, health, and environment. The project is assessing policy options for livestock industry management in light of the scientific knowledge available about ecosystems and health. The goal is to optimize the potential for creating win-win scenarios that support economic development, poverty reduction, health, and environmental protection.

Туре	Intervention	Targets	Products
Community education	behavioral change, application of all other interventions	all vectors	
Environmental management	natural environment changes	mosquitoes, blackflies, snails, etc.	
and sanitation	improved housing quality	vectors of Chagas disease, malaria, dengue	
	physical barriers to breeding sites	vectors of filariasis, trachoma	polystyrene beads in standing water bodies
Biological control	larvivorous fishes	mosquitoes	
	predators and competitors	snails	
	larviciding	urban mosquitoes, blackflies	microbial larvicides, organophosphates, neem extracts and other herbal insecticides
Chemical control	space spraying	urban mosquitoes	pyrethroids, organophosphates
	indoor residual spraying	vectors of malaria, lymphatic filariasis, leishmaniasis	pyrethroids, organophosphates, carbamates, DDT (malaria only)
	insecticide-treated materials	vectors of malaria, leishmaniasis, lymphatic filariasis, trypanosomiasis	pyrethroids
	household products	mosquitoes, flies, fleas	aerosols, coils, mats, repellents, natural products, etc.

Table 12.2. Components of Integrated Vector Control (based on WHO 2003, p. 5)

tion, for example through deforestation or irrigation schemes, probably has more widespread effects on infectious disease transmission. This highlights the importance of considering vectorborne diseases within any development that causes a large-scale change to the physical environment.

There are, however, specific cases where environmental modification has been used successfully to destroy either vector or reservoir host habitat, particularly at the fringes of disease transmission. Although destructive locally, careful targeting can minimize environmental impacts. Successful examples include draining, filling, or raising brackish breeding sites of the coastal malaria vector *An. sundaicus* in Indonesia in the 1940s (Takken et al. 1991) or, more recently, the filling of peri-urban breeding sites for malaria vectors in Zambia and India (Baer et al. 1999). In each of these areas, incidence of malaria declined significantly.

Temporary changes to the environment are often termed environmental manipulation. These include flushing streams or canals, providing intermittent irrigation to agricultural fields such as rice, temporarily flooding or draining wetlands, or removing specific types of vegetation that provide larval habitats for mosquitoes. A combination of vegetation clearance, modification of river boundaries, increasing velocity of the river flow to interrupt larval development, and swamp drainage were highly successful complements to bed nets and insecticide spraying in Zambia in the early twentieth century (Utzinger et al. 2001, 2002). Intermittent irrigation has proven successful in controlling *Anopheles* in ricegrowing regions in India, China, and other parts of Asia (Pal 1982; Lacey and Lacey 1990), and clearance of algae from rivers has been effective in reducing malaria transmission in Oaxaca, Mexico (IDRC 2003).

For zoonotic diseases (those with a non-human reservoir host of infection), environmental management techniques can be applied to reduce the abundance of the reservoir host as well as the vector. For example, cutaneous leishmaniasis due to *Leishmania major* in the former Soviet Union has been controlled by plowing up or flooding of colonies of the reservoir host, the great gerbil *Rhombomys opimus*. (See Box 12.2.) Crucially, well-targeted environmental management techniques can be highly cost-effective. The analysis of malaria control in the Zambian copper belt indicated that the cost-effectiveness of sustained environmental interventions (\$22–92 per healthy life saved) were comparable to those from insecticide-based methods, even excluding valuation of the reduced environmental impacts (Utzinger et al. 2001).

#### 12.3.3 Biological Control/Natural Predators

Biological methods consist of the utilization of biological toxins and natural enemies to achieve effective vector management. Targeted biological control using larvivorous fish and copepods as well as the toxic products of bacterial agents has been successfully used to control vectors of filariasis and malaria, and notably vectors of dengue in Viet Nam (reviews by Walker 2002; Lloyd 2003). An important advantage over chemical methods is the reduction in ecosystem disturbance. Microbial larvicides can be safely added to drinking water and in environmentally sensitive areas, as they do not persist or accumulate in the environment or in body tissues and are not toxic to vertebrates (WHO 1999). Also, there is no evidence that native (as opposed to exotic) larvivorous fish pose any threat to local biodiversity or the safety of drinking water.

Biological control may be effective if breeding sites are well known and limited in number but less feasible where they are numerous. Biological control thus provides a good illustration of the importance of knowledge of local transmission ecology. Economic incentives may also be important in spurring initial interest in biological control mechanisms. In Asia, for instance, larvivorous fish have been effective where pisciculture can provide additional economic, agricultural, and nutritional benefits (Wu et al. 1991; Gupta et al. 1992; Victor et al. 1994). In China, Wu et al. (1991) found that stocking rice paddies with edible fish improved rice yield, supported significant fish production, and greatly reduced the number of malaria cases (Walker 2002). Community participation and inte-

	Disease	Ecosystem Service				
Response		Food	Fresh Water	Biodiversity	Cultural Services	Wood (Forestry)
Insecticidal sprays	malaria, African sleeping sickness, leishmaniasis, filariasis, Chagas, trypanosomiasis, West Nile virus, dengue	Ļ	Ţ	Ţ		
Larviciding	dengue, malaria, onchocerciasis	$\downarrow$	$\downarrow$	$\downarrow$		
Insecticide-treated bednets	malaria, Leishmaniasis					
Traps/targets	African sleeping sickness, leishmaniasis					$\downarrow$
Larvivorous fish	malaria, dengue	<b>↑</b>	<b>↑</b>	$\downarrow$		
Bacillus sphaericus	filariasis		$\downarrow$	$\downarrow$		
Rodent/reservoir control	leishmaniasis			$\downarrow$		
Killing hosts	dracunculiasis, schistosomiasis	$\downarrow$				
Surveillance Chemotherapy/chem oprophylaxis	all diseases malaria, schistosomiasis, onchocerciasis, lymphatic filariasis (humans)	↓ (livestock)			Ţ	
	African sleeping sickness, hydatid disease (animals)					
Vaccines	yellow fever				↑	
Personal protection	dengue, malaria, leishmaniasis				↑	
Improved housing construction	Chagas					$\downarrow$
Environmental management	malaria, dengue, schistosomiasis		ſ	Î	1	
Irrigation/impoundment/ swamp drainage	schistosomiasis, malaria	$\downarrow\uparrow$	$\downarrow\uparrow$	$\downarrow$		
Improvement in sanitation and hygiene practices	ectoparasitic diseases, gastrointestinal helminth parasites	Ţ	Î		Ť	
Health education	all diseases				Ţ	

#### Table 12.3. Ecosystem Services Affected by Responses to Vector-borne Diseases

gration with other control methods are important, as larvivorous fish and other biological agents may need repeated restocking/ reapplication, and in some cases vegetation clearance or removal of pollution sources to maintain their habitat.

#### 12.3.4 Chemical Control

Chemical control methods of malaria vector management can potentially be organized quickly, and can be highly cost-effective if used efficiently. The advent of insecticides in the 1940s, with the widespread use of dichlorodiphenyltrichloroethane (DDT), resulted in less emphasis on environmental and biological methods of control and the reliance, for a period of two decades, on insecticides. The WHO Malaria Eradication Campaign of the 1950s achieved eradication in several sub-tropical regions and controlled malaria transmission on much of the Indian subcontinent for several years. More recently, insecticide-based campaigns have had notable success in reducing transmission of Chagas disease in the southern cone region and elsewhere in Latin America (see Box 12.3), while the Onchocerciasis Control Program eliminated the disease from much of the program area using various insecticides in rotation. (See Box 12.4.)

Widespread application of persistent insecticides was initially undertaken with little regard for environmental consequences. Evidence has since accumulated of the wider environmental effects of insecticide spraying (for example, impacts of pyrethroid spraying against tsetse on river fauna such as Crustaceans (Molyneux et al. 1978) and poisoning of reservoirs), and greater attention is now paid to using knowledge of the ecology of vectors to develop more cost-effective and less environmentally damaging methods of application by using less toxic or persistent chemicals. Various delivery methods have thus been developed. The insecticide may be applied as a non-residual application (effective over a short time-scale, killing only insects currently exposed) or a residual (persistent) application, effective over a period of weeks or months. The latter application may kill even those insects that were in immature stages of development, and not directly exposed to the insecticide at the time of application. Synthetic pyrethroid treated nets, used in the control of malaria and other vector-borne diseases, are one example of such an approach, which has a minimal impact on broader ecosystems. Information on when and where particular vector species tend to rest and feed (indoors or outdoors) and whether they feed on humans or other animals also helps to target spraying efforts.

Certain chemical insecticides can also be safely applied to larval breeding sites. For example, temephos exhibits very low mammalian toxicity and has been used for malaria control in India

#### Environmental Management of Zoonotic Cutaneous Leishmaniasis in Central Asia

In the deserts of Turkmenistan, Uzbekistan, southern Kazakhstan, and southern Tajikistan in Central Asia, the distribution of zoonotic cutaneous leishmaniasis, caused by the protozoan parasite Leishmania major, is largely dependent on the distribution of the great gerbil Rhombomys opimus (Sergiev 1979; Saf'Janova 1985). This is a relatively large (200 gram) diurnal rodent that lives in family groups in vast underground burrow systems, each occupying an area of around 1,000-3,000 square meters, with around 300-400 meters of passages up to three meters in depth, with openings to the surface every one to two meters (WHO 1990). Each complex typically houses five to ten rodents during the summer months, before the young disperse; in suitable habitats, there are two to three burrow complexes per hectare. Hence, R. opimus has a dominant influence on the environment, with the burrows providing an enormous haven of constant temperature and humidity occupied by more than 50 species of vertebrates and hundreds of invertebrates. Among the many parasites that find hosts and are transmitted in the burrows, L. major is the most widely distributed, typically infecting 30-50% of R. opimus across its range.

The burrows provide optimal conditions for the principal sand-fly vector of *L. major, Phlebotomus papatasi.* Like all sand flies, the larvae are terrestrial and live in moist organic matter. The sand flies overwinter as diapausing fourth instar larvae, the adults emerging after the soil temperature reaches 20° Celsius at a depth of 50 centimeters. Adult sand flies rest during the day in the well-insulated burrows and feed at night. *P. papatasi* has a noted host preference for the great gerbil, being especially attracted to its fleshy ears, which when infected by *L. major* generate long-lasting non-ulcerating lesions which can be infective to sand flies for up to two years (Sergiev 1979). Parasites can therefore survive in great gerbils during the winter (that is, between transmission seasons).

Most human cases in this region are due to infections in oases located in the river valleys and foothill plains of southern Turkmenia and Uzbeki-

and Mauritius (Kumar et al. 1994; Gopaul 1995), in the Onchercerciasis Control Program, and is widely applied to potable water to control *Aedes aegypti*. In contrast, synthetic pyrethroids are effective but are problematic as larvicides due to their frequent high toxicity to aquatic non-target organisms (Chavasse and Yap 1997).

Insecticides therefore remain an important tool and their selective use is likely to continue within IVM. However, there are concerns over the impacts of insecticides, especially the persistent organic pollutants identified in the Stockholm Convention, on the natural environment and on exposed human populations, particularly insecticide sprayers (Chavasse and Yap 1997). There is, as well, growing evidence of insect resistance to insecticides. Such developments led to World Health Assembly resolution WHA 50.13, which called on member states to support the development and adoption of viable alternative methods of controlling vectorborne diseases and thereby reducing reliance on insecticides. IVM provides a management framework for cost-effective, rational, and environmentally sensitive use of insecticides until they can be phased out without exposing populations to increased disease risk.

# 12.4 Social and Behavioral Responses to Vectorborne Disease

An ecosystems perspective views the human cultural, social, and behavioral environment as integral to the sustainability of critical stan (Sergiev 1979; Saf'Janova 1985). But humans are accidental "deadend" hosts of L. major, playing no role in maintaining the transmission cycle. Hence, the highly successful Soviet Union-run control program to reduce the risk of ZCL (notably during its large programs of land reclamation in Central Asia) used to focus on rodent control. This program utilized a remarkably effective and relatively inexpensive environmental intervention that dramatically decreased the capacity of the environment to maintain the transmission cycle of L. major. Rodent control was achieved by three methods (Vioukov 1987; WHO 1990): complete plowing up of burrows (as in the Golodnava Steppe in Uzbekistan); crushing of burrows with wide-track heavy caterpillar tractors (as in Turkmenia); and the use of poisoned bait (as in Karshinskaya Steppe, Uzbekistan). This latter intervention can be highly efficient. One group of three to four men can destroy all the gerbils in an area of 50,000 hectares in one season. Transmission of ZCL halted over 900 square kilometers in the Karshinskaya Steppe by poison baits after a three-year control program. For all three methods, the impact is only transitory if rodents are allowed to immigrate into the treated areas from untreated territories. Permanent environmental control is only achievable by preventing reinvasion by physical barriers, such as canals or vast agricultural fields.

Although the intervention unavoidably affects the local habitat, efforts were made to reduce wider impacts. In order to address concerns that the poison baits would affect non-target animals (birds and cattle), baits were introduced into the rodent burrows at a depth of 15–20 centimeters subsequently filling up the burrow (Saf'Janova 1985). In addition, habitats targeted for intervention are targeted by using large-scale photography to identify where burrows are likely to be and to exclude unsuitable sites—then possible sites are surveyed and burrows mapped. After treatment, follow-up surveys are conducted and treatments repeated if necessary (Vioukov 1987).

ecosystem services. This is particularly true in the case of vectorborne diseases, which are profoundly influenced by human patterns of settlement and behavior. Social and behavioral resources and tools are therefore increasingly recognized as relevant to the management of vector-borne disease. Improved disease control may be achieved by changing human behavior or settlement patterns in ways that reduce contact with vectors.

#### 12.4.1 Human Settlement Patterns

Probably the most basic way in which human-vector contact may be managed is via improvements in the placement and construction of housing settlements (Rozendaal 1997). Although individual vectors are often able to disperse many kilometers, in many situations the majority of the vector population moves only a very small distance within its lifetime. Thus the abundance of insect populations can vary markedly even within a very small distance. Locating settlements on well-drained, high ground more than one to two kilometers away from major breeding sites may significantly reduce transmission of diseases such as malaria (WHO 1982). In many cases, however, housing sites are determined by other imperatives (such as the need to be close to a water source). Aedes vectors are particularly well adapted to breeding in urban areas, particularly in household water containers. Therefore, screening of windows, eaves, and doors to protect people from bites can help prevent the spread of the disease from infected human reservoir hosts, and improved household management of

#### International Initiatives to Control Trypanosomiasis

Sustainable control of vector-borne diseases is rarely achievable through small-scale intervention projects from actors outside of the local community, such as government Ministries or international agencies. This is because once an intervention project ends, or political interest wanes, the treated area remains at risk of reinfestation from untreated regions. This has been a marked problem for the control of tsetse-borne trypanosomiasis in Africa, where premature curtailment of intervention projects—even where highly successful—has typically seen steady recrudescence of transmission as tsetse returned to the project areas.

A similar problem is faced in the control of American trypanosomiasis (Chagas disease), which is by far the most socioeconomically significant parasitic disease of Latin America. Although effective methods to halt transmission by eliminating domestic vector populations have been known since the 1950s, the ease with which vectors can be passively transported from one region to another made small-scale interventions unsustainable. Even when Brazil launched a highly successful national campaign against Chagas disease transmission in 1983, it was clearly recognized that similar interventions would need to be carried out at least along the frontier regions of neighboring Argentina, Bolivia, Paraguay, and Uruguay. But even with frontier intervention agreements, the Brazilian national campaign encountered an additional problem affecting continuity. In 1986, due to changing political priorities, all 600 staff engaged in Chagas disease control in rural areas were switched to mosquito control in urban centers. The Chagas disease control program was suspended.

This experience highlighted several key points. At the technical level, it was clear that the intervention techniques and operational strategy were highly effective, while population genetic studies strongly supported the idea that a sustainable end-point could be reached through eradication of all domestic populations of the main vectors. At the political level, however, there was a clear need to find ways of maintaining continuity until that end-point could be reached, as well as a need to promote similar interventions in neighboring countries in order to eliminate all risk of reinfestation.

The enlightened response came in 1991 with a joint agreement be-

tween ministries of health of the six southernmost countries of Latin America (Argentina, Bolivia, Brazil, Chile, Paraguay, and Uruguay) to implement simultaneous interventions against Chagas disease. This program—the Southern Cone Initiative—was joined by Peru in 1996 to encompass the entire geographic distribution of the main vector, *Triatoma infestans*. All countries implement similar interventions but retain national autonomy for financing and operational approaches. Coordination is provided by the Pan American Health Organization through a system of national evaluations carried out by teams drawn from the Chagas control services of neighboring countries. By 1997, Uruguay became the first of these countries to be formally certified free of Chagas disease transmission, followed by Chile in 1999, most of the central and southern states of Brazil in 2000/1, and the first four provinces of Argentina in 2002. More provinces in Argentina and several departments in Paraguay and Bolivia are also being evaluated for similar certification.

The Southern Cone Initiative has yet to reach its final objective of eliminating all domestic populations of Triatoma infestans and halting Chagas disease transmission throughout the program area, some 6 million square kilometers. And it has not been without economic and political difficulties, especially the economic instability of recent years and the problems arising from decentralization of executive services. But this successful model of regional collaboration focused on a biologically defined target has paved the way for similar initiatives against Chagas disease in Central America and the Andean Pact countries (both formally launched in 1997) and in Mexico and the Amazon region. Significantly, the model has also been taken up by African countries with the launch of the Pan African Initiative against tsetse and trypanosomiasis (PATTEC) launched by the Organization of African Unity (now called the African Union) at the 2000 summit in Lomé, Togo. PATTEC represents a vision to eliminate tsetse and trypanosomiasis transmission from the whole of Africa, not by small donor-led projects but by a series of regional initiatives focused on biologically defined targets: when a vector population is eliminated over its entire range, transmission is halted and cannot be restarted by that population.

stored water (for example, putting lids on storage jars) can eliminate vector-breeding sites.

Improving housing construction is particularly important for protection against infections such as Chagas disease, where the vectors live directly in the walls of poor houses. Housing improvements shown to reduce Chagas-vector contact with humans include concrete floors, plaster and brick walls, and tiled roofs (De Andrade et al. 1995); these obviously have co-benefits in terms of raising overall living conditions. Studies in Sri Lanka have indicated that residents of poorly constructed houses were as much as 2.5 times more likely to contract malaria than neighbors in houses of good construction (Gamage-Mendis et al. 1991; Gunawardena et al. 1998). Economic analysis in Sri Lanka indicated that government investments to improve the most vulnerable houses would be compensated by savings in malaria treatment within eight years (Gunawardena et al. 1998).

Zooprophylaxis (using diversionary hosts to reduce the proportion of bloodmeals taken on humans, and thus cutting disease transmission) is also a promising tool. This technique usually makes use of domestic livestock that also provide other services such as milk and labor and causes minimal ecosystem disruption. It does, however, require knowledge of local vector ecology to select and site diversionary hosts, to ensure that increased provision of bloodmeals does not increase local vector density to an extent that outweighs the reduced proportion of bites on humans. It has been demonstrated to be effective in Indonesia (Kirnowor-doyo and Supalin 1986), the Philippines (Schultz 1989), and Sri Lanka (van der Hoek et al.1998). In the most endemic regions of sub-Saharan Africa, there is some evidence for effectiveness against *Anopheles arabiensis*, but there may be fewer prospects for use against the more anthropophagic (human-biting) *Anopheles gambiae*. (See Box 12.5.)

#### 12.4.2 Health Awareness and Behavior

Vector-borne diseases such as malaria may be more serious when the victim is malnourished, in ill health, or suffering from gastrointestinal diseases. Thus there is a strong link between overall social well-being and disease impact. In particular, improved awareness of hygiene and sanitation, particularly among women, may be important in reducing infectious disease among children. General educational levels, particularly of women, are a key determinant of awareness of health risks, and therefore health status.

In addition to general education improvements, however, messages specifically targeted at behavioral changes associated with vector protection are important tools in disease prevention,

#### Monitoring and Managing Environmental Effects of Insecticidal Control of Onchocerciasis in Africa

Onchocerciasis can be combated by appropriate vector control operations which consist of arresting transmission of the parasite by eliminating the vector population for the duration of the lifespan of the adult worm from the human reservoir host. This has been applied and demonstrated in parts of the original area of the Onchocerciasis Control Program in West Africa, where vector control alone has been carried out for more than fourteen consecutive years and where the disease is no longer a public health problem (Hougard et al. 2001). As black fly adults are difficult to target, the vector control operations consist of treating with appropriate insecticides the breeding sites of rivers where the reophilic larval stages develop.

The mere fact of regularly using insecticides for many years raised the concern of the potential risk such operations could have for the aquatic environment. Indeed, at the time OCP was launched, there was much evidence on biological and ecological consequences of DDT. With the awareness of the "DDT syndrome" by the international community, the participating countries as well as the donors that support the program (28 countries and foundations) had reasons to fear that repeated application of insecticides in the water courses would cause serious disturbances of the freshwater ecosystems. In 1974, just before the beginning of operational activities, OCP set up an aquatic monitoring program of rivers planned to be regularly treated with insecticides (Lévêque et al. 1979). It was implemented to satisfy three major concerns:

- to provide early warning to those carrying out treatments if toxic effects were noticed in the short term and to ensure that the insecticide release did not excessively disturb the functioning of the treated ecosystems on a long-term basis (the expected duration of OCP);
- to avoid the widespread use of chemicals that might have adverse effects on human populations near the river systems and/or might accumulate in the food chain as DDT has been known to do; and
- to prevent the irreversible loss of aquatic biodiversity in West Africa both because freshwater fish are a major source of food as well as

an economic activity for West African populations, and to meet the objective of the Convention on Biodiversity that stipulates that countries are responsible for the conservation of their biodiversity.

The OCP in West Africa closed in December 2002, after 29 years of activity. There is no equivalent of a public health program benefiting from such long-term financial support from the international community. One reason for this support was that OCP always convinced the donors of the effectiveness of the control strategies used. The other reason was the OCP's ongoing to take care of the aquatic environment with the involvement of national teams and international expertise. The implementation of a long-term monitoring program to assess the potential effects of larvicid-ing and the large-scale screening of larvicides to select that which is most efficient for *Simulium* while less drastic for the non-target fauna are unique features in large health control programs. These efforts had an economic cost in terms of insecticide consumption and operational strategies but they made it possible to preserve the quality of the water used by the riverine populations as well as the fishing resources that constitute a significant part of the foodstuff of these populations.

The goal has been achieved: onchocerciasis has been virtually eliminated from the OCP area as a disease of public health importance and as an obstacle to socioeconomic development. From the environmental point of view, the success of OCP may be jeopardized by an unsustainable use of the freed land. For example, a pilot study conducted in the Léraba area showed that 75% of the original wooded savanna was cleared for agricultural development and settlement of villages (Baldry et al. 1995). The riverine forests of many small rivers were destroyed and on some of the banks soil erosion is occurring. On the other hand, the bordering forests and the easily flooded plains of the larger rivers did not undergo any disturbance of this scale. It is therefore necessary to both take measures and sensitize the riverine populations on the need for environmental protection and biodiversity management along with the development of agricultural activities.

particularly for diseases such as dengue that lack vaccines or curative drugs. Simple poster displays in local languages can be highly effective. These may include messages such as the early identification of disease symptoms; the need to maintain attendance for drug delivery; and refraining from interfering with traps for vectors such as tsetse.

Such messages may in some cases be backed up by legislation (for example, fines for not removing potential dengue-breeding sites). In many cases, however, they will be most effective when they are developed in a participatory manner, using methods that involve the community in the identification of problems and solutions. Depending on the situation, they may best be disseminated via a range of media, such as posters, community events, or presentations, or by including the subject in popular radio or television programs such as soap operas. It should also be noted that behavioral changes may be impossible if they are not supported by government services; for example, poor urban populations will be unwilling or unable to remove dengue-breeding sites if there is no garbage collection service or reliable water supply.

The effectiveness of environmental health education in changing behavior is often measured through knowledge, attitude, and practice surveys, and ultimately through changing disease rates. KAP studies for dengue control in the Caribbean have indicated that, while knowledge has increased with respect to vector control, there is not much evidence of this knowledge being put into action (Polson et al. 2000). In many cases, people do not take action because they believe that mosquito control is the responsibility of the government (Rosenbaum et al. 1995). In addition, even community members who rid their own premises of mosquito habitats may suffer from the inaction of less vigilant neighbors, necessitating combined community efforts. While community participation and inter-sectoral collaboration is therefore perceived as a positive approach, they are challenging tasks and require concerted sustained effort by key stakeholders and professionals as well as government.

# 12.5 "Cutting-edge" Interventions: Genetic Modification of Vector Species to Limit Disease Transmission

In the short term, the largest strides in vector control and management may come from applied research that refines existing tools and targets them more effectively to local situations. Such applications may also be highly cost-effective. However, new tools, while requiring substantially greater investment of time and resources in order to overcome initial technical barriers, can potentially result in dramatic improvements in control. For example,

### Integrated Vector Management Strategies for Malaria

IVM strategies for controlling malaria are receiving renewed attention globally among scientists, health officials, and policy-makers. This is due to the rapid spread of resistance to antimalarial drugs such as chloroquine and the apparent inability of past large-scale eradication campaigns to even hold the disease in check let alone eliminate transmission in the regions where it is most endemic, such as Africa. Indeed, over 1.2 million people, overwhelmingly African children, died from malaria in 2002, an increase in mortality in absolute terms over the previous year (WHO 2003, 2004a). There is also concern over potential vector resistance against pesticides commonly used for indoor residual spraying and insecticide-treated materials.

These limitations have spurred interest in integrated approaches to malaria vector control (Walker 2002). IVM approaches hold the potential to significantly reduce if not interrupt disease transmission as well as the burden of serious disease and death, while avoiding very severe disruptions to ecosystem services.

Environmental modification strategies, such as the drainage of wetlands, were among the first employed to deliberately control malaria vectors nearly a century ago. Of increasing interest today are strategies for less intrusive changes in wetlands environments—improving the flushing of streams or removing vegetation from water to limit the breeding areas where larvae may develop. In areas where dams and reservoirs are to be constructed, there is evidence that better engineering design of dams or irrigation schemes, to provide for alterations in level and flow of water, the flushing of reservoirs, and periodic weed removal can minimize the development of new vector habitats. Options for the best-practice design of dams and agricultural irrigation projects to control vector breeding sites, while minimizing the disruption to ecosystem services, are detailed in Tiffen (1991); Birley (1991); and Phillips et al. (1993).

In tropical Africa, where malaria is most endemic, IVM strategies may be most relevant in areas of less intense transmission and in peri-urban or urban locales, where breeding sites may be fewer, most easily identifiable, and more amenable to control (Walker 2002). Particularly in such settings, there is evidence that incremental reductions in vectorial capacity, while not eradicating the disease may play a role in reducing morbidity and mortality and improving health in specific age groups, that is, pregnant women and children under the age of two. For larvae control in such settings, greater attention is being given to the efficacy of biological controls such as larvivorous fish and biolarvicides, that is, *Bacillus thurengiensis israelensis* and *sphaericus* (Walker 2002).

However, in rural areas of intense malaria transmission, a better understanding of relationships between human habitats, farming, and livestock practices, may provide important tools for controlling malaria using IVM methods, and in a manner that sustains positive ecosystem services. For instance, alternating between cycles of irrigated and non-irrigated crops may disrupt breeding cycles (Tiffen 1991; Mutero et al. 2004). Better management and control of manmade sites where malarial mosquitoes may easily reproduce such as water bore holes may help reduce malaria breeding close to human settlements. Conversely, more strategic placement of new human settlements away from potential malaria breeding areas can also reduce transmission (Walker 2002). Recent research in Kenva on the interactions between malaria, livestock, and agriculture has highlighted the potential for livestock to act as "diversionary hosts" for certain species of malaria vectors. The study, conducted in four villages of the Mwea Division of Kenya, found malaria disease prevalence was significantly lower in the two villages with rice irrigation schemes than in the villages with no irrigated agriculture (0-9% versus 17-54%). The lower incidence occurred despite the existence of a 30-300 fold increase in the number of local malaria vectors in the irrigated locales. The likely explanation for the so-called "paddies paradox" appeared to be the tendency for the prevalent A. arabiensis vector to feed overwhelmingly on cattle rather than on humans (Mutero et al. 2004).

At the same time, advances in geographical information systems together with continuing research into vector entomology are permitting more precise mapping of vector species composition, spatial distribution, and transmission patterns. This is contributing to a better understanding of vector ecology, that may be used to guide control operations that maximize the use of targeted control strategies and minimize ecosystem disruptions (Shililu et al. 2003a, 2003b).

there is a need to develop new curative drugs and insecticides to both overcome problems of vector resistance and reduce disease control costs, while the development of an effective vaccine could potentially revolutionize control of malaria.

In addition to developing "new varieties of old tools," there is the potential for developing qualitatively different types of tools, with very different implications both for disease control and other ecosystem services. Genetic modification of vectors is one such method.

The practice of selecting strains of vectors that are unable to transmit disease has been applied for several decades (Collins et al. 1986; Wu and Tesh 1990). However, recent advances in molecular genetics have made it potentially much more feasible to introduce genes into vector populations that either drive the population to extinction or that reduce their capacity to maintain and transmit infections. These include the sequencing of the full genome of the malaria vector *Anopheles gambiae* (Holt et al. 2002), the stable introduction of engineered genetic constructs into the genome of a number of important mosquito species (for example, Coates et al. 1998; Catteruccia et al. 2000; Allen et al. 2001; Grossman et al. 2001), and the identification and activation of genetic constructs that block or reduce pathogen transmission of

malaria parasites and dengue viruses in mosquitoes (for example, de Lara Capurro et al. 2000; Ito et al. 2002).

It is therefore theoretically possible to produce in the laboratory mosquito populations that are unable to transmit important pathogens. The next stage is to implement "gene-driving" mechanisms, which link the genes of interest to other genetic elements that have the ability to spread throughout the vector population, from initial seeding releases. Two main drive systems are under investigation. The first consists of autonomous transposable elements (Ribeiro and Kidwell 1994), genetic elements that copy themselves throughout the genome, thereby increasing the chance of inheritance into the next generation. The second is symbiotic Wolbachia bacteria, which are inherited through egg cells and give host females a reproductive advantage over uninfected females (Sinkins and O'Neill 2000). Genetic mechanisms that reduce or block pathogen transmission could thus be attached to such a driver in order to achieve maximum dissemination in the vector population.

Major technological challenges remain in the completion of all the stages described above in a single vector population (for example, Alphey et al. 2002). In addition, some disease control experts are concerned about the application of transgenic tools. They highlight the potential that the transposable elements could also increase mutation rates, with unforeseen characteristics in the vector populations, and that genetically engineered constructs could cross-contaminate other species. They also stress that it may prove more difficult than assumed to spread the relevant genes through highly variable populations of parasites or vectors. Ethical issues are also involved, most importantly that it will be essential to achieve broad informed consent of the populations who will come into contact with the vector populations, as there would be no option for individuals to "opt out" of the intervention (Scott et al. 2002). Critics who raise these issues generally stress the importance of using existing tools in a wider, more sustained and targeted manner rather than developing new interventions (Curtis 2000).

Supporters of transgenic techniques point out that the kinds of inherited elements being discussed are not normally horizontally transferred between individuals, even of the same species, so that crossing species boundaries would presumably be an even more rare event (for example, O'Neill et al. 1997). If, indeed, such transfer did occur, there would be no reason to expect that an element specifically designed to interfere with pathogenmosquito interactions would have any effects in non-target species. In addition, gene spreading mechanisms such as transposable elements and *Wolbachia* are very common in natural insect populations, and have had no detectable long-term effects on host ecology (for example, Turelli and Hoffmann 1991; Kidwell 1992). They therefore conclude that the risks of negative environmental impact associated with the kinds of replacement strategies that are being developed are low.

There is, as yet, no firm consensus among researchers on the practicality and acceptability of applying these tools in the field. As they develop further, it will become more important for the scientific community to present a rational and dispassionate view of the potential benefits and threats of this approach to decisionmakers and the public so that they may be better positioned to judge whether the possible gains from this type of intervention outweigh any environmental risks.

# 12.6 Promoting Inter-sectoral Cooperation among Health, Environment, and Development Institutions

An ecosystems perspective on vector-borne disease control requires a reconsideration of institutional structures that manage vector control overall. Integrated vector management, in particular, operates on the premise that effective control requires the collaboration of various public and private agencies as well as community education and participation rather than exclusive action by the health sector. This is part of an increasing appreciation that the Millennium Development Goals for infectious diseases (and other goals) will only be achievable with contributions from health, environment, and development institutions at global, national, and local levels.

Yet, present institutional structures tend to promote a narrow sectoral and disease-specific approach to interventions. In most countries, health and environment sectors remain divided, with little coordination of approaches to vector control and associated energy, agricultural, housing, and forestry policies. Health sector institutions often leverage significant resources, but their actions tend to be directed towards curative treatment or interventions against specific diseases, rather than promoting integrated policies for economic development, environmental protection, and improved human health. The environment sector typically has access to fewer financial resources and political power, and focuses mainly on protection of the natural environment. Productive sectors, such as ministries of infrastructure, development, or trade, often access significant resource pools and take decisions that have profound influences (both positive and negative) on the transmission of vector-borne diseases, but these are not considered systematically. As a result, there is seldom an incentive for, for example, a malaria control program to carry out interventions that protect against other human diseases, protect the environment, or promote, say, agricultural development. Inter-sectoral collaboration is thus "blessed by everybody and funded by nobody"; it is widely acknowledged as essential, but rarely occurs because individual sectors measure success only against their own targets.

Institutionally, it is often easier to design and assess the success of "top-down" control campaigns that motivate political will and raise resources, with clear lines of institutional responsibility and measurable targets to reach a highly specific goal. In many instances, such programs have been successful, when directly judged against their stated aims (that is, eradication or specific levels of reduction).

However, such approaches have seldom led to complete eradication of a disease. This can be due to the slackening of political will once the initial visible gains of the "attack phase" have been achieved and the limits recognized of promoting a single intervention uniformly rather than a range of locally adaptable approaches. The greater use of "sector-wide approaches" to financing rather than individual project funding by international donors (Cassels 1997) and greater involvement of nongovernmental actors (such as charitable NGOs and the private sector) have also made centrally organized national or international control campaigns more difficult to execute. In a related development, the decentralization of decision-making within developing countries has resulted in the dismantling of centralized vector control mechanisms upon which control campaigns may rest, making participatory approaches far more relevant.

The advantages and disadvantages of campaign-style sectoral approaches and newer, more inter-sectoral and participatory approaches are illustrated by the Caribbean experience with dengue control. Prior to 1962, several Caribbean islands, along with most of mainland Latin America, had succeeded in eradicating the Aedes aegypti mosquito, vector of dengue and yellow fever, following an intensive eradication campaign. This success was attributed to centralized, vertically structured programs; use of DDT and adequate funding for insecticides; and the availability of equipment and well-trained staff. This success was, however, not sustained mainly because it was not possible to maintain the effectiveness of the limited number of control methods used (insecticide and source reduction) and achieve eradication in all countries of the region. When Ae. aegypti subsequently reinvaded from neighboring countries, another eradication campaign was deemed as unfeasible because of increased urbanization that had led to structural inadequacies in the provision of basic services such as garbage collection and piped water. In addition, chronic economic crises in many of the most affected countries had led to decreased capacity and political prioritization for vector control programs.

In 1992, the Pan American Health Organization in collaboration with the government of Italy and the Caribbean Cooperation in Health initiated a five-year project whose general objective was to reduce the densities of *Ae. aegypti* in fifteen English-speaking Caribbean countries to a level at which transmission of the dengue virus will not occur. The project aimed to strengthen existing national vector control programs using community participation as the focus. As a result of the project, programs in some countries, including St. Vincent and the Grenadines, shifted away from the traditional "top-down" approach to one of community involvement and partnership. Collaboration between vector control programs and environmental health programs was improved, and the scope of control was broadened to include control of pests and vectors other than *Ae. aegypti*. It should be noted, however, that there is as yet no evidence that this approach has led to a sustained decrease in the persistently high levels of *Ae. aegypti* disease in the countries involved outside the time frame of the original project.

In other settings, however, such as Viet Nam, a national approach to dengue management, based upon community participation and involvement, seems to have had greater and more sustained success. (See Box 12.6.) In small-scale projects in Ghana, an integrated community approach to malaria intervention measures has been reported to result in reduction of overall child mortality by as much as 50% (Curtis 1991).

Despite the general lack of inter-sectoral and community cooperation in vector-borne disease management, there are some promising developments. In recent decades, agencies such as the World Bank, UNICEF, and UNDP have increasingly invested in global health issues. This reflects a growing institutional recognition that healthier people are more productive, and ill health both creates and maintains poverty. The result has been several new interagency initiatives in the environment, health, and development arena. These include the WHO Commission on Macroeconomics and Health, and joint WHO and UNEP initiatives promoting linkages between environment and health in awareness raising, monitoring, and policymaking. The World Health Organization and the USAID-supported Environmental Health Project have collaborated with governments and other key international stakeholders to develop a global strategy for integrated vector management, along with practical guidelines and training tools, as an important component of the Roll Back Malaria Campaign. This initiative has already had marked success in bringing together multiple ministries in several African countries to develop "national consensus statements" on how each agency can contribute to addressing malaria. There are now also legal requirements that large-scale development projects (particularly those funded by agencies such as the World Bank or international development banks) carry out environmental impact assessments that also include consideration of human health impacts (for ex-

#### BOX 12.6

#### Advances in the Targeted Control of Mosquito Vectors of Dengue

Dengue fever and associated dengue hemorraghic fever is the world's fastest growing vector-borne disease and the most important vector-borne *viral* disease affecting humans. Dengue is found in nearly one hundred tropical countries and is responsible for the loss of over 19,000 lives and 610,000 disability adjusted life years (DALYs) annually (Lloyd 2003; WHO 2004a).

In the 1960s, *Aedes aegypti* eradication campaigns, aimed against the urban yellow fever mosquito, which also is the principal dengue-carrying vector, succeeded in eliminating the mosquito from most of Latin America. But it has resurfaced in the past three decades, and is currently found throughout much of the tropics and sub-tropics. Urbanization and population movement are responsible for much of the recent resurgence. The epidemiology and ecology of dengue is complicated by the fact that there are four primary serotypes of the disease, some or all of which may be circulating in a particular endemic region at a particular time. When a serotype is introduced to a population with low herd immunity, epidemics may occur when vector densities are relatively low. Among vulnerable populations, serial exposure to more than one dengue serotype increases, rather than reduces, the risk of severe illness (Halstead 1988).

Around human settlements, Ae. aegypti mosquitoes breed primarily in artificial water containers, and the mosquito's life cycle is closely associated with human activities. Larval habitats are increasing rapidly with unplanned urbanization and greater amounts of water-retaining waste products that provide a habitat for mosquitoes (Lloyd 2003). Rising global temperatures and humidity may further increase dengue disease incidence (Hales et al. 2002), as Aedes mosquitoes reproduce more quickly and bite more frequently at higher temperatures (Patz et al. 2003). Since there is no curative treatment for dengue, targeted environmental and ecosystem management is all the more relevant. However, in many settings, community cleanup campaigns or space-spray application of insecticides, using either pyrethroids or organophosphates, have had limited or only temporary effects on disease incidence. Recently, there has been increasing interest in identifying the most productive mosquito breeding sites and in better understanding epidemiological knowledge about the thresholds below which mosquito densities have to be reduced in order to prevent a severe outbreak.

More recently, the work of Focks et al. has led to the development of predictive computer models that may accurately determine a "threshold" limit for epidemic risk in a particular locale. This relatively inexpensive model considers local levels of population immunity to various dengue serotypes, as well as vector densities and ambient temperature, to yield a calculation of the threshold number of *Aedes* pupae (effectively equivalent to adult numbers) per person per area (Focks et al. 2000) to maintain transmission.

The same authors have also designed inexpensive household surveys that more precisely identify the most productive containers, or breeding sites, containing the highest densities of *Ae. aegypti* pupae. These are the containers from which significant numbers of adult mosquitoes are likely to emerge. Similar tools, key container and key premise indices, have been developed and tested in Viet Nam (Nam 2003). The development of such models and new indices has paralleled a growing awareness that less than 1% of the containers may produce more than 95% of the adult mosquitoes that trigger disease outbreaks. So once the most productive containers are identified, targeted environmental management of dengue becomes more affordable and feasible. Targeted vector control also minimizes disruption to other ecosystem services.

Control strategies may include more community cleanup aimed specifically at the types of containers most closely associated in the local setting with vector breeding and disease transmission, such as old tires or discarded water drums (Hayes et al. 2003). In addition, biological and targeted chemical methods of control are being used with increased precision. In Viet Nam, for instance, a small crustacean, Mesocyclops (Copepoda), which feeds on the newly hatched larvae of Ae. aegypti, has been introduced into household water tanks and water jars in three northern provinces; the intervention is reported to have resulted in eradication or near eradication of Aedes larvae in treated areas (Nam 2003). In Cambodia, WHO is testing, together with national and local authorities, a new long-lasting insecticide-impregnated net mesh water tank cover, using the same approach to water containers now commonly used with insecticidetreated bednets in malaria control. The cover, fitted over concrete rainwater storage tanks, is designed both to prevent mosquito breeding in these key containers and to reduce adult vector densities and longevity.

ample, consideration of the effects of dam construction on vectorborne disease).

Most importantly, a number of "bottom-up" inter-sectoral collaborations in developing countries have shown promising results against several vector-borne diseases. For example, a CGIAR System-wide Initiative on Malaria and Agriculture is exploring the links between irrigation practices, livestock practices, and malaria disease transmission and incidence in seven African countries and settings, using a transdisciplinary "ecosystems" approach. This approach emphasizes the importance of understanding socioeconomic factors, such as gender issues, substance abuse, and malnutrition, that may contribute to greater disease incidence and severity. It also stresses participatory methods that involve the local community as partners in vector and disease control, together with researchers and policymakers. This is part of a wider drive towards stakeholder-driven transdisciplinary work under the Ecosystem Approaches to Human Health initiative at Canada's International Development Research Centre (IDRC 2004).

# 12.7 Analysis and Assessment of the Different Responses

There is now significant experience from various parts of the world with integrated "ecosystems" approaches to vector management and control. These indicate that a more systematic use of existing scientific knowledge about vector behavior, within an ecosystems framework, may cost-effectively reduce disease burdens. At the same time, this approach may offer greater protection to other ecosystems services than has been obtained in the past from vertical "campaign-oriented" programs.

IVM strategies are promising not because they apply new and different interventions but because they provide a structure for selecting and applying the most effective existing intervention, given local epidemiological and ecological characteristics. This includes targeting control efforts in space and time, and toward specific stages of the lifecycle of vectors. There has been an additional emphasis on more precisely characterizing epidemiological zones. Geographic information systems can be useful in defining such zones and the distribution of different vector species, which may be more or less amenable to specific control interventions. IVM strategies may still rely quite heavily on the use of insecticides. These can be applied in ways that have minimal impact on the wider environment, particularly for diseases with a humanvector/human-transmission cycle (for example, use of insecticidetreated bed nets or residual spraying inside houses to control malaria), although focused application is often more difficult when the transmission cycle includes animal reservoir hosts of infection. Although these chemicals still may impact on health and environment, the relatively small amounts used, and accurate targeting, means that these effects are likely to be much smaller than those from agricultural application of pesticides. Insecticide resistance is a threat to the long-term sustainability of chemical interventions, and needs to be managed. However, there remain very few examples where it has seriously undermined control programs. While the limited use of organochloride compounds such as DDT has also been permitted under the Stockholm Convention for indoor residual spraying against malaria, a more widespread use of IVM strategies may help reduce reliance on chemical interventions.

Participatory mechanisms and behavioral tools can be important to promoting vector management at the community level, within an ecosystem framework. It is important, however, to evaluate the effectiveness of various social responses and approaches in reducing clinical disease. Behavioral changes are notoriously difficult to sustain. Some challenges are specific to particular diseases, such as the need to reduce *Aedes* populations down to specific, and generally very low, levels in order to have a significant impact on dengue transmission. Others can be extrapolated more widely. These include difficulties in engendering interest in community-wide behavioral change; what to do when noncompliance by individuals puts others at risk; and the problems in sustaining behavioral change over time, particularly when the disease transmission threat is relatively low, to prevent reemergence of disease threats or invasion from other regions.

Along with better applied use of existing knowledge and technologies, basic research into radically different approaches may yield new tools for vector management or control over the long term. For example, research into the development of transgenic vectors is a promising new avenue that could potentially allow for the inexpensive replacement of existing vector populations with vectors that are incapable of disease transmission. However, time and financial resources are necessary to overcome various technical barriers. Secondly, there is an ongoing debate over the wider ecological and ethical implications of such introductions, as shown by the controversy over the introduction of genetically modified foods in some societies. The debate largely reflects different values rather than disputes over the scientific evidence. Proponents can demonstrate that there is no a priori reason to expect harmful consequences, while opponents focus on the difficulty of proving long-term safety or reversing an introduction if negative effects are detected.

Strategies to reduce infectious disease transmission should ideally be quantified in terms of overall social and economic benefits to human populations. Outcomes often remain narrowly defined and success is measured against a small set of indicators. Interventions made through the health sector often are judged primarily in terms of effectiveness in cutting incidence rates or curing disease cases—in some cases with associated measures of economic costs. While these are clearly critical considerations and are also important for making comparisons between similar kinds of health system interventions, such an assessment tends to downplay the ways a given health system intervention or policy may impact other ecosystems services. Thus important "externalities" are often ignored because they are displaced and diffused over time, geographical settings, and the affected populations, and therefore difficult to quantify.

At the same time, policy responses that have nothing to do with health overtly, often have powerful indirect impacts on ecosystem services and infectious disease rates which may also vary in time and space, and be even more difficult to assess and quantify. For example, there is clear evidence that aspects of climate regulation and biodiversity are linked to infectious disease transmission. Policies that impact climate change and biodiversity, either positively or negatively, will therefore also have an impact ultimately on disease incidence and health. It is often only possible to assess those global effects in general terms. Overall, however, policies promoting sustainable development, by increasing individual and societal wealth while decreasing inequalities and avoiding degradation of natural resources, can benefit both human and ecosystem health.

Institutional responses are clearly critical in the design of such integrated policies. Initiatives to build capacity and synergies across institutional sectors face great challenges, in design, implementation, and assessment. Inter-sectoral collaborations may yield the greatest overall benefits to society but are seldom the best way for individual sectors to demonstrate their performance. For example, ministries of health may still gain more credit for improving treatment rates for a particular disease than for collaborating with ministries of environment to ensure sustainable development and protection of natural resources, even if the latter approach yields greater overall societal benefits in the long run. Thus inter-sectoral collaboration on vector-borne disease management will be achievable only through sustained high levels of awareness and participation from intergovernmental, governmental, and donor agencies.

#### References

- Allen, M.L., D.A. O'Brochta, P.W. Atkinson, and C.S. Levesque, 2001: Stable, germ-line transformation of Culex quinquefasciatus (Diptera: Culicidae), *Journal of Medical Entomology*, 38, pp. 701–10.
- Alphey, L., C.B. Beard, P. Billingsley, M. Coetzee, A. Crisanti, et al., 2002: Malaria control with genetically manipulated insect vectors, *Science*, 298, pp. 119–21.
- Baer, F., C. McGahey, and P. Wijeyaratne, 1999: Summary of EHP activities in Kitwe, Zambia, 1997–1999: Kitwe Urban Health Programs, US Agency for International Development, Environmental Health Project, Arlington, VA.
- Baldry, D., D. Calamari, and L. Yaméogo, 1995: Environmental impact assessment of settlement and development of the Upper Léraba basin, World Bank, Washington, DC, pp. 1–38.
- Birley, M., 1991: Guidelines for Forecasting the Vector-borne Disease Implications of Water Resources Development, WHO, Geneva, Switzerland/ Food and Agriculture Organization of the United Nations, Rome, Italy/ United Nations Environment Programme, Nairobi, Kenya/ United Nations Center for Human Settlements, Geneva, Switzerland.
- Campbell-Lendrum, D., J.P. Dujardin, E. Martinez, M.D. Feliciangeli, J.E. Perez, et al., 2001: Domestic and peridomestic transmission of American cutaneous leishmaniasis: Changing epidemiological patterns present new control opportunities, *Memorias de Instituto Oswaldo Cruz*, 96, pp. 159–62.
- **Cassels,** A., 1997: A Guide to Sector-wide Approaches for Health and Development: Concepts, Issues and Working Arrangements, WHO, Danish International Development Agency, Department for International Development, European Commission, Geneva, Switzerland.
- Catteruccia, F., T. Nolan, T.G. Loukeris, C. Blass, C. Savakis, F.C. Kafatos, et al., 2000: Stable germline transformation of the malaria mosquito Anopheles stephensi, *Nature*, 405, pp. 959–62.
- Chavasse, D. and H. Yap (eds.), 1997: Chemical Methods for the Control of Vectors and Pests of Public Health Importance, WHO, Geneva, Switzerland.
- Coates, C.J., N. Jasinskiene, L. Miyashiro, and A.A. James, 1998: Mariner transposition and transformation of the yellow fever mosquito, Aedes aegypti, *Proceedings of the National Academy of Sciences, USA*, 95, pp. 3748–51.
- Collins, F.H., R.K. Sakai, K.D. Vernick, S. Paskewitz, D.C. Seeley, et al., 1986: Genetic selection of a Plasmodium-refractory strain of the malaria vector Anopheles gambiae, *Science*, 234, pp. 607–10.
- Curtis, C., 1991: Control of Disease Vectors in the Community, Wolfe Publishing, London, UK.
- Curtis, C.F., 2000: Infectious disease: The case for deemphasizing genomics in malaria control, *Science*, 290, p. 1508.
- **De Andrade**, A.L., F. Zicker, R.M. De Oliveira, I.G. Da Silva, S.A. Silva, et al., 1995: Evaluation of risk factors for house infestation by *Triatoma infestans* in Brazil, *American Journal of Tropical Medicine and Hygiene*, **53**, pp. 443–7.
- de Lara Capurro, M., J. Coleman, B.T. Beerntsen, K.M. Myles, K.E. Olson, et al., 2000: Virus-expressed, recombinant single-chain antibody blocks sporozoite infection of salivary glands in Plasmodium gallinaceum-infected Aedes aegypti, American Journal of Tropical Medicine and Hygiene, 62, pp. 427–33.
- Focks, D.A., R.J. Brenner, J. Hayes, and E. Daniels, 2000: Transmission thresholds for dengue in terms of Aedes Aegypti Pupae per person with discussion of their utility in source reduction efforts, *American Journal of Tropical Medicine and Hygiene*, **62**, pp. 11–8.
- Gallup, J.L. and J.D. Sachs, 2001: The economic burden of malaria, American Journal of Tropical Medicine and Hygiene, 64, pp. 85–96.
- Gamage-Mendis, A.C., R. Carter, C. Mendis, A.P. De Zoysa, P.R. Herath, et al., 1991: Clustering of malaria infections within an endemic population: Risk of malaria associated with the type of housing construction, *American Journal of Tropical Medicine and Hygiene*, **45**, pp. 77–85.
- Gopaul, R., 1995: [Entomological surveillance in Mauritius], Santé, 5, pp. 401–5.
- Grossman, G.L., C.S. Rafferty, J.R. Clayton, T.K. Stevens, O. Mukabayire, and M.Q. Benedict, 2001: Germline transformation of the malaria vector, Anopheles gambiae, with the piggy-back transposable element, *Insect Molecular Biology*, **10**, pp. 597–604.

- Gubler, D.J., 1997: Human behavior and cultural context in disease control, Tropical Medicine and International Health, 2, pp. A1–2.
- Gunawardena, D.M., A.R. Wickremasinghe, L. Muthuwatta, S. Weerasingha, J. Rajakaruna, et al., 1998: Malaria risk factors in an endemic region of Sri Lanka, and the impact and cost implications of risk factor-based interventions, *American Journal of Tropical Medicine and Hygene*, 58, pp. 533–42.
- Gupta, D.K., R.M. Bhatt, R.C. Sharma, A.S. Gautam, and Rajnikant, 1992: Intradomestic mosquito breeding sources and their management, *Indian Journal of Malariology*, 29, pp. 41–6.
- Gwatkin, D.R., M. Guillot, and P. Heuveline, 1999: The burden of disease among the global poor, *Lancet*, 354, pp. 586-9.
- Hales, S., N. de Wet, J. Maindonald, and A. Woodward, 2002: Potential effect of population and climate changes on global distribution of dengue fever: An empirical model, *Lancet*, 360, pp. 830–4.
- Halstead, S.B., 1988. Pathogenesis of dengue: Challenges to molecular biology, Science, 239, pp. 476–81.
- Hay, S.I., D.J. Rogers, S.E. Randolph, D.I. Stern, J. Cox, et al., 2002: Hot topic or hot air? Climate change and malaria resurgence in East African highlands, *Trends in Parasitology*, 18, pp. 530–4.
- Hayes, J.M., E. Garcia-Rivera, R. Flores-Reyna, G. Suarez-Rangel, T. Rodriguez-Mata, et al., 2003: Risk factors for infection during a severe dengue outbreak in El Salvador in 2000, *American Journal of Tropical Medicine and Hy*giene, 69, pp. 629–33.
- Hewitt, S. and M. Rowland, 1999: Control of zoophilic malaria vectors by applying pyrethroid insecticides to cattle, *Tropical Medicine and International Health*, 4, pp. 481–6.
- Holt, R.A., G.M. Subramanian, et al., 2002: The genome sequence of the malaria mosquito Anopheles gambiae, *Science*, 298: pp. 129–49.
- Hougard, J.M., E.S. Alley, L. Yameogo, K.Y. Dadzie, and B.A. Boatin, 2001: Eliminating onchocerciasis after 14 years of vector control: A proved strategy, *Journal of Infectious Diseases*, **184**, pp. 497–503.
- **IDRC** (International Development Research Centre), 2003: Malaria Control in Coastal Oaxaca, Mexico, IDRC, Ottawa, OT, Canada.
- **IDRC,** 2004: *Ecosystems Approaches to Human Health*, IDRC, Ottawa, ON, Canada.
- Ijumba, J.N., F.C. Shenton, S.E. Clarke, F.W. Mosha, and S.W. Lindsay, 2002: Irrigated crop production is associated with less malaria than traditional agricultural practices in Tanzania, *Transactions of the Royal Society of Tropical Medicine and Hygene*, 96, pp. 476–80.
- IPCC (Intergovernmental Panel on Climate Change), 2001: Climate Change 2001: The scientific basis, Contribution of Working Group 1 to the Third Assessment Report of the IPCCC, Cambridge University Press, Cambridge, UK.
- Ito, J., A. Ghosh, L.A. Moreira, E.A. Wimmer, and M. Jacobs-Lorena, 2002: Transgenic anopheline mosquitoes impaired in transmission of a malaria parasite, *Nature*, 417, pp. 452–5.
- Jetten, T. and W. Takken, 1994: Anophelism without malaria in Europe: A review of the ecology and distribution of the genus Anopheles in Europe, Wageningen Agricultural University Papers, Wageningen, The Netherlands, pp. 1–69.
- Kidwell, M.G., 1992: Horizontal transfer of P elements and other short inverted repeat transposons, *Genetica*, 86, pp. 275–86.
- Kirnowordoyo, S., and Supalin, 1986: Zooprophylaxis as a useful tool for control of A. aconitus transmitted malaria in Central Java, Indonesia, *Journal of Communicable Diseases*, 18, pp. 90–4.
- Kovats, R.S., D.H. Campbell-Lendrum, A.J. McMichael, A. Woodward, and J.S. Cox, 2001: Early effects of climate change: Do they include changes in vector-borne disease? *Philosophical Transaction of the Royal Society of London Series B - Biological Sciences*, 356, pp. 1057–68.
- Kuhn, K.G., D.H. Campbell-Lendrum, B. Armstrong, and C.R. Davies, 2003: Malaria in Britain: Past, present, and future, *Proceedings of the National Academy of Sciences*, **100**, pp. 9997–10001.
- Kumar, A., V.P. Sharma, P.K. Sumodan, D. Thavaselvam, and R.H. Kamat, 1994: Malaria control utilizing Bacillus sphaericus against Anopheles stephensi in Panaji, Goa, *Journal of the American Mosquito Control Association*, **10**, pp. 534–9.
- Lacey, L.A. and C.M. Lacey, 1990: The medical importance of riceland mosquitoes and their control using alternatives to chemical insecticides, *Journal of* the American Mosquito Control Association Supplement, 2, pp. 1–93.
- Lévêque, C., M. Odei, and M. Pugh Thomas, 1979: The Onchocerciasis Control Programme and the monitoring of its effects on riverine biology of the Volta River Basin. In: *Ecological Effects of Pesticides*, F. Perring and K. Mellanby (eds.), Academic Press, New York, NY, pp. 133–43.

- Lloyd, L., 2003: Best Practice for Dengue Prevention and Control in the Americas, Environmental Health Project, USAID (Agency for International Development), Washington, DC.
- Lopez, A.D. and C.C. Murray, 1998: The global burden of disease, 1990–2020, *Nature Medicine*, **4**, pp. 1241–43.
- McMichael, A.J., 2001: Human Frontiers, Environments and Disease: Past Patterns, Uncertain Futures, Cambridge University Press, Cambridge, UK.
- Molyneux, D.H., 1997: Patterns of change in vector-borne diseases, Annals of Tropical Medicine and Parasitology, 91, pp. 827–39.
- Molyneux, D.H., 2003: Common themes in changing vector-borne disease scenarios, *Transactions of the Royal Society of Tropical Medicine and Parasitology*, 97, pp. 129–32.
- Molyneux, D.H., D.A. Baldry, P. De Raadt, C.W. Lee, and J. Hamon, 1978: Helicopter application of insecticides for the control of riverine Glossina vectors of African human trypanosomiasis in the moist savannah zones, *Annales de la Societe Belge de Medecine Tropicale*, 58, pp. 185–203.
- **Murray**, C. and A. Lopez (eds.), 1996: *The Global Burden of Disease*, World Health Organization, Harvard School of Public Health, World Bank, Geneva, Switzerland.
- Mutero, C., C. Kabutha, V. Kimani, L. Kabuage, G. Gitau, et al., 2004: A transdisciplinary perspective on the links between malaria and agroecosystems in Kenya, *Acta Tropica*, 89, pp. 171–86.
- Nam, V.S., 2003: Key container and key premise indices for Ae. aegypti surveillance and control. In: Best Practices for Dengue Prevention and Control in the Americas, L. S. Lloyd (ed.), Environmental Health Project, US Agency for International Development, Washington, DC, pp. 51–6.
- **Newton**, E.A. and P. Reiter, 1992: A model of the transmission of dengue fever with an evaluation of the impact of ultra-low volume (ULV) insecticide applications on dengue epidemics, *American Journal of Tropical Medicine and Hygene*, **47**, pp. 709–20.
- **O'Neill**, S., A. Hoffmann, and J. Werren, 1997: Influential passengers: Inherited microorganisms and arthropod reproduction, Oxford University Press, Oxford, UK.
- Pal, R., 1982: Disease vector control in the People's Republic of China, Mosquito News, 42, pp. 149–58.
- Patz, J., A.K., M. Githeko, J.P. McCarty, S. Hussain, U. Confalonieri, et al., 2003: Climate change and infectious diseases. In: *Climate Change and Human Health: Risks and Responses*, A. McMichael, D. Campbell-Lendrum, C. Corvalan, K. Ebi, A. Githeko, et al. (eds.), WHO, Geneva, Switzerland.
- Patz, J.A., T.K. Graczyk, N. Geller, and A.Y. Vittor, 2000: Effects of environmental change on emerging parasitic diseases, *International Journal of Parasitol*ogy, 30, pp. 1395–405.
- Phillips, M., A. Mills, and C. Dye, 1993: Guidelines for Cost-Effectiveness Analysis of Vector Control, WHO, Geneva, Switzerland/Food and Agriculture Organization of the United Nations, Rome, Italy/ United Nations Environment Programme, Nairobi, Kenya/ United Nations Centre for Human Settlements, Geneva, Switzerland.
- Pitt, S., B.E. Pearcy, R.H. Stevens, A. Sharipov, K. Satarov, et al., 1998: War in Tajikistan and re-emergence of Plasmodium falciparum, *Lancet*, 352, p. 1279.
- Polson, K., S. Rawlins, D. Chadee, and C. Brown, 2000: A case-control study of Dengue fever cases in Trinidad in 1997, *West Indian Medical Journal*, 49(Suppl. 2), pp. 58–9.
- Reiter, P., 2000: From Shakespeare to Defoe: Malaria in England in the Little Ice Age, *Emerging Infectious Diseases*, **6**, pp. 1–11.
- Reiter, P., 2001: Climate change and mosquito-borne disease, *Environmental Health Perspectives*, **109(Suppl. 1)**, pp. 141–61.
- Reiter, P., S. Lathrop, et al., 2003: Texas lifestyle limits transmission of Dengue virus, *Emerging Infectious Diseases*, **9**, pp. 86–9.
- Ribeiro, J.M. and M.G. Kidwell, 1994: Transposable elements as population drive mechanisms: Specification of critical parameter values, *Journal of Medical Entemology*, **31**, pp. 10–6.
- Rosenbaum, J., M.B. Nathan, R. Ragoonanansingh, S. Rawlins, C. Gayle, et al., 1995: Community participation in dengue prevention and control: A survey of knowledge, attitudes, and practice in Trinidad and Tobago, *American Journal of Tropical Medicine and Hygene*, 53, pp. 111–7.
- Rowland, M. and F. Nosten, 2001: Malaria epidemiology and control in refugee camps and complex emergencies, *Annals of Tropical Medicine and Parasitol*ogy, 95, pp. 741–54.
- Rowland, M., N. Durrani, M. Kenward, N. Mohammed, H. Urahman, and S. Hewitt, 2001: Control of malaria in Pakistan by applying deltamethrin insecticide to cattle: A community-randomised trial, *Lancet*, 357, pp. 1837–41.
- **Rozendaal,** J., 1997: Vector Control: Methods for Use by Individuals and Communities, WHO, Geneva, Switzerland.

- Saf'Janova, V., 1985: Leishmaniasies in the USSR. In: *Leishmaniasis*, K. Chang and R. Bray (eds.), Elsevier, Amsterdam, The Netherlands.
- Sampaio, L., 1951: Medicina rural: O aparecimento, a expansão e o fim da leishmaniose no estado de São Paulo, *Revista Brasileira de Medicina*, 8, pp. 717–21.
- Schultz, G.W., 1989: Animal influence on man-biting rates at a malarious site in Palawan, Philippines, *Southeast Asian Journal of Tropical Medicine and Public Health*, 20, pp. 49–53.
- Scott, T.W., W. Takken, B.G. Knols, and C. Boete, 2002: The ecology of genetically modified mosquitoes, *Science*, 298, pp. 117–9.
- Sergiev, V., 1979: Epidemiology of leishmaniasis in the USSR. In: *Biology of the Kinetoplastida*, H. Lumsden and D. Evans (eds.), Academic Press, London, UK.
- Shililu, J., T. Ghebremeskel, S. Mengistu, H. Fekadu, M. Zerom, et al., 2003a: Distribution of anopheline mosquitoes in Eritrea, American Journal of Tropical Medicine and Hygene, 69, pp. 295–302.
- Shililu, J., T. Ghebremeskel, S. Mengistu, H. Fekadu, M. Zerom, et al., 2003b: High seasonal variation in entomologic inoculation rates in Eritrea, a semiarid region of unstable malaria in Africa, *American Journal of Tropical Medicine* and Hygene, 69, pp. 607–13.
- Sinkins, S. and S. O'Neill, 2000: Wolbachia as a vehicle to modify insect populations, *Insect Transgenesis: Methods and Applications*, CRC Press, Boca Raton, FL.
- Takken, W., W.B. Snellen, J.P. Verhave, B.G.J. Knols, and S. Atmosoedjono, 1991: Environmental Measures for Malaria Control in Indonesia: An Historical Review on Species Sanitation, Agricultural University Wageningen, Wageningen, The Netherlands.
- Thomson, C., J. Harper, and M. Begon, 2000: *Essentials of Ecology*, Blackwell Science, Oxford, UK.
- Tiffen, M., 1991: Guidelines for the Incorporation of Health Safeguards into Irrigation Projects through Intersectoral Cooperation, WHO, Geneva, Switzerland/ Food and Agriculture Organization of the United Nations, Rome, Italy/ UN Environmental Programme, Nairobi, Kenya/ UN Centre for Human Settlements(Habitat), Geneva, Switzerland.
- Turelli, M. and A.A. Hoffmann, 1991: Rapid spread of an inherited incompatibility factor in California Drosophila, *Nature*, 353, pp. 440–2.
- Utzinger, J., Y. Tozan, and B.H. Singer, 2001: Efficacy and cost-effectiveness of environmental management for malaria control, *Tropical Medicine and International Health*, 6, pp. 677–87.
- Utzinger, J., Y. Tozan, F. Doumani, and B.H. Singer, 2002: The economic payoffs of integrated malaria control in the Zambian copperbelt between 1930 and 1950, *Tropical Medicine and International Health*, **7**, pp. 657–77.
- van der Hoek, W., F. Konradsen, D.S. Dijkstra, P.H. Amerasinghe, and F.P. Amerasinghe, 1998: Risk factors for malaria: A microepidemiological study in a village in Sri Lanka, *Transactions of the Royal Society of Tropical Medicine* and Hygiene, 92, pp. 265–9.
- Victor, T.J., B. Chandrasekaran, and R. Reuben, 1994: Composite fish culture for mosquito control in rice fields in southern India, *Southeast Asian Journal of Tropical Medicine Public Health*, 25, pp. 522–7.
- Vioukov, V., 1987: Control of transmission. In: The Leishmaniases in Biology and Epidemiology, W. Peters and R. Killick-Kendrick (eds.), Academic Press, London, UK.
- Walker, K., 2002: A Review of Control Methods for African Malaria Vectors, Environmental Health Project, US Agency for International Development, Washington, DC.
- Walsh, J.F., D.H. Molyneux, and M.H. Birley, 1993: Deforestation: Effects on vector-borne disease, *Parasitology*, 106(Suppl.), pp. S55–75.
- WHO (World Health Organization), 1982: Manual for Environmental Management for Mosquito Control, with Special Emphasis on Malaria Vectors, WHO, Geneva, Switzerland, 281 pp.
- **WHO**, 1990: Control of the Leishmaniases, Report of a WHO Expert Committee, WHO, Geneva, Switzerland.
- WHO, 1999: Bacillus Thurinigiensis, Environmental Health Criteria, WHO, Geneva, Switzerland, 217 pp.
- WHO, 2001: The World Health Report 2001: Mental Health: New Understanding, New Hope, WHO, Geneva, Switzerland.
- WHO, 2003: Guidelines for Integrated Vector Management, WHO Regional Office for Africa, Harare, Zimbabwe.
- WHO, 2004a: The World Health Report 2004: Changing History, WHO, Geneva, Switzerland.
- **WHO**, 2004b: *Global Strategic Framework for Integrated Vector Management*, WHO, Geneva, Switzerland.

- Wilder-Smith, A., W. Foo, A. Earnest, S. Sremulanathan, and N.I. Paton, 2004: Seroepidemiology of dengue in the adult population of Singapore, *Tropical Medicine and International Health*, **9**, pp. 305–8.
- **Wu**, N., G.H. Liao, D.F. Li, Y.L. Luo, and G.M. Zhong, 1991: The advantages of mosquito biocontrol by stocking edible fish in rice paddies, *Southeast Asian Journal of Tropical Medicine and Public Health*, **22**, pp. 436–42.
- Wu, W.K. and R.B. Tesh, 1990: Selection of Phlebotomus papatasi (Diptera: Psychodidae) lines susceptible and refractory to Leishmania major infection, *American Journal of Tropical Medicine and Hygiene*, 42, pp. 320–8.
- Zavaleta, J.O. and P.A. Rossignol (2004): Community-level analysis of risk of vector-borne disease, *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 98(10), pp. 610–8.